

**Serum inhibins A and B fall differentially as FSH rises in perimenopausal women.**

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BACKGROUND: Serum FSH levels rise with increasing age in normal women, particularly as they enter the menopausal transition and progress to the **postmenopausal** state. The contributions of decreasing levels of inhibin-A (INH-A) and inhibin-B (INH-B) to this rise are presently unclear, as there are no reports of dimeric INH levels in relation to menopausal status. The present study was undertaken in order to provide preliminary data on relationships amongst the dimeric inhibins, oestradiol (E2) and FSH in normal subjects of defined menopausal status. METHODS: Single serum samples were obtained between cycle days 3 and 8 in regularly cycling women, or at random in those with irregular cycles or amenorrhoea, in 110 women, aged 48-59 years, in the third year of a prospective longitudinal study of the menopausal transition, 'The Melbourne Women's Mid-Life Health Project'. Samples were **assayed** for FSH, E2, INH-A, INH-B and immunoreactive inhibin (IR-INH) and results were analysed following logarithmic transformation. Undetectable values were assigned the limit of sensitivity of the respective **assays**. The relationships between hormones were evaluated as a function of menopausal stage. The latter was assigned as Stage 1, **premenopausal** (no reported change in menstrual cycle pattern), Stage 2, early peri-menopausal (reported change in menstrual cycle frequency in the preceding year with a bleed in the preceding 3 months), Stage 3, late peri-menopausal (no menses in the preceding 3-11 months) and Stage 4, **postmenopausal** (no menses in the preceding 12 months). RESULTS: The **hormone** concentrations in **premenopausal** subjects (geometric means, FSH 13.5 IU/l, E2 306 pmol/l, IR-INH 217 U/l, INH-A 96 ng/l, and INH-B 48 ng/l) were used as reference points for the other stages of menopausal status. Early peri-menopausal subjects had significantly lower levels of IR-INH (147 U/l) and INH-B (13.5 ng/l) in the presence of a small, statistically nonsignificant rise in FSH (to 21.4 U/l) and no significant change in E2 or INH-A. In late peri-menopausal subjects, IR-INH fell to 76 U/l, INH-A fell to 4.2 ng/l, whilst INH-B was not significantly different at 14 ng/l. FSH had risen significantly to 72.21 U/l. Oestradiol also fell significantly to 89 pmol/l. In the **postmenopausal** subjects there were no further significant changes in the peptide hormones or FSH, but E2 fell further to 41 pmol/l. There was a significant ( $P < 0.05$ ) inverse correlation between FSH and E2 ( $R = -0.78$ ), FSH and IR-INH ( $R = -0.66$ ), FSH and INH-A ( $R = -0.53$ ), FSH and INH-B ( $R = -0.29$ ) while IR-INH and either INH-A or INH-B were positively correlated ( $R = +0.57$  and  $+0.35$ , respectively). The data are consistent with negative feedback roles for both dimeric inhibins and E2 as contributors to the regulation of FSH secretion as menopausal status changes. CONCLUSIONS: The major significant endocrine event in women in the early peri-menopausal phase of the menopausal transition is a substantial fall in the circulating levels of inhibin-B with no significant change in inhibin-A or oestradiol. Progression to late peri-menopausal status is accompanied by a marked fall in inhibin-A and oestradiol and a rise in FSH without further change in inhibin-B. Inhibin-B, a marker of follicle number, is a significant factor in the endocrinology of the menopausal transition.

Tags: Female; Human; Support, Non-U.S. Gov't

Descriptors: Follicle Stimulating **Hormone** --blood--BL; \*Inhibins--blood--BL; \*Peptides--blood--BL; \* **Premenopause** --blood--BL; \*Prostatic Secretory Proteins; Cross-Sectional Studies; Estradiol--blood--BL; Middle Aged; Prospective Studies

between the threshold and ceiling level for monofollicular growth. This threshold level is surpassed intentionally during IVF treatment cycles to induce multiple follicular recruitment. The threshold level can change under situations such as polycystic ovaries, **perimenopause**, oral contraceptives, and GnRH analogue treatment. CONCLUSIONS: To avoid the risk of ovarian hyperstimulation syndrome and multiple pregnancies, careful adjustments of serum FSH levels should be made by fine dosage modifications. By monitoring FSH levels and using less **sialylated** preparations, the efficacy of the treatment probably will improve. (62 Refs.)

Tags: Female; Human; Male

Descriptors: \*Follicle Stimulating Hormone--pharmacokinetics--PK; Animals; Follicle Stimulating Hormone--metabolism--ME; Follicle Stimulating Hormone--therapeutic use--TU; Gonadotropins--therapeutic use--TU; Ovulation Induction; Polycystic Ovary Syndrome--drug therapy--DT; Recombinant Proteins

CAS Registry No.: 0 (Gonadotropins); 0 (Recombinant Proteins); 9002-68-0 (Follicle Stimulating Hormone)

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**Serum concentrations of dimeric inhibins, activin A, gonadotrophins and ovarian steroids during the menstrual cycle in older women.**

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The transition from regular ovarian cyclicity to menopause is associated with a rise in the circulating concentrations of follicle stimulating hormone (FSH), despite the maintenance of serum oestradiol concentrations during the **perimenopause**. The aim of this study was to compare the pattern of secretion of dimeric inhibins, activin A, gonadotrophins and steroids in regularly cycling women of 40-50 years with normal and raised early follicular phase serum FSH concentrations and young women (25-33 years) during the menstrual cycle. Blood samples were taken prospectively almost daily throughout the menstrual cycle. Women recruited were classified into three groups: (i) older women with normal FSH [(ON-FSH), day 3 FSH <8 mIU/ml, n = 10]; (ii) older women with raised FSH [(R-FSH), day 3 FSH >8 mIU/ml, n = 6] and (iii) young normal FSH (YN-FSH) women, age 25-32 years (n = 6). Cyclic patterns of serum inhibins and activin A were similar in the ON-FSH and YN-FSH groups. The R-FSH group had significantly lower concentrations of inhibin A prior to the luteinizing hormone (LH) surge and in the mid-luteal phase and lower concentrations of inhibin B in the early follicular phase compared with the ON-FSH group. Serum concentrations of activin A, progesterone and oestradiol were similar in all three groups. It is concluded from this study that the rise in early follicular phase serum FSH in older women is associated with a decrease in circulating concentrations of inhibin B in the early follicular phase. However, lower circulating concentrations of inhibin A in the luteal phase of the R-FSH group may also contribute to the rise in early follicular phase FSH concentrations during the menstrual cycle, although further studies with larger numbers are required to confirm this observation.

Tags: Comparative Study; Female; Human; Support, Non-U.S. Gov't

Descriptors: \*Gonadotropins--blood--BL; \*Inhibins--blood--BL; \*Menstrual Cycle--physiology--PH; \*Steroids--blood--BL; Activins; Adult; Age Factors;

CAS Registry No.: 0 (Peptides); 0 (Prostatic Secretory Proteins); 0 (inhibin-alpha subunit); 0 (prostatic secretory protein PSP94); 50-28-2 (Estradiol); 57285-09-3 (Inhibins); 9002-68-0 (Follicle Stimulating Hormone)

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**Ovarian testosterone secretion during perimenopause .**

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OBJECTIVE: The aim of the study was to investigate ovarian **testosterone** secretion during the last few years of reproductive life and after menopause. MATERIALS AND METHODS: Ovarian and peripheral venous levels of total **testosterone** were analyzed in 52 women aged 42-69 years (mean 51) undergoing hysterectomy with adnexal removal for benign indications at the Department of Obstetrics and Gynecology at Tampere University Hospital, Finland. The study population was divided into pre- (n = 19), peri- (n = 18) and **postmenopausal** (n = 15) women in addition to the classical division according to menstrual cycle. Corresponding serum estradiol, progesterone and **gonadotropin** levels were **measured**, and the degree of ovarian stromal hyperplasia was analyzed. RESULTS: The levels of all steroid hormones were higher in the ovarian vein than in the periphery. A significant positive correlation was found between age and ovarian vein **testosterone** levels (r = 0.3, P = 0.01). In **premenopausal** women, it was 1.5 nmol/l (median; range 0.78-6.0), in **perimenopausal** women 2.2 nmol/l (range 0.9-13.6), and 2.5 nmol/l (range 0.6-26.6) in **postmenopause**, respectively. Peripheral **testosterone** level did not increase with age. Ovarian stromal hyperplasia was significantly associated with increased **testosterone** secretion (P = 0.009). CONCLUSION: The ovary seems to increase the secretion of **testosterone** into circulation during the menopausal transition period, as the highest levels were **measured** in **postmenopausal** women. High **testosterone** levels in the ovarian vein, however, were not reflected in the peripheral venous blood.

Tags: Female; Human

Descriptors: Menopause--blood--BL; \*Ovary--secretion--SE; \* **Testosterone** --secretion--SE; Adult; Aged; Gonadal Steroid Hormones--blood--BL; Menstrual Cycle--blood--BL; Middle Aged; Reference Values; Secretory Rate --physiology--PH

CAS Registry No.: 0 (Gonadal Steroid Hormones); 58-22-0 (Testosterone)

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